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EXAMINER	
MCGILLEM, LAURA L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,320	DOHMER ET AL.	
	Examiner	Art Unit	
	Laura McGillem	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 November 2001* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-18 are pending.

Priority

It is acknowledged that the instant application is a National Stage Application of PCT/DE01/00597, filed 02/15/2001.This application receives benefit of priority to German Patent No. 100 12 220.5, dated 3/14/2000.

Information Disclosure Statement

The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of

determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a).

Specification

The disclosure is objected to regarding the Brief Description of the Drawings because Figure 5 includes several nucleotide sequences that have not been identified by SEQ ID NOs. Correction is required.

The specification is objected to because Applicants have submitted the sequences of 19 synthetic oligonucleotides but they are not mentioned by SEQ ID NO in the text of the specification.

Claim Objections

Claims 1-18 are objected to because of the following informalities: The claims do not begin with the word " A" or "An" or "The". Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 10-13 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under

35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claims 1-5, 8 and 10-15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 1 is drawn to a test system expressing at least three cytochrome P450 2D6 alleles. As written, the claims read on products of nature such as a tissue, an intact animal or human.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The invention appears to employ biological material, specifically the cell lines V79MZh2D6*1, V79MZh2D6*2, V79MZh2D6*9, V79MZh2D6*10 and V79MZh2D6*17. Since the biological material is essential to the claimed invention, it must be obtainable by a repeatable method set for the in the specification or otherwise readily available to the public. If the biological material is not so obtainable or available to the public, the

requirements of 35 USC 112 may be satisfied by a deposit of the biological material. The specification does not disclose a repeatable process to obtain the biological material and it is not apparent if the biological material is readily available to the public. It is noted that the Applicants have deposited the biological material on Feb. 15, 2000, at the DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH under the accession numbers DSM ACC2446, DSM ACC2447, DSM ACC2448, DSM ACC2449 and DSM ACC2450, but there is no indication in the specification as to public availability. If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the cell line has been deposited under the Budapest Treaty and that the cells will be irrevocably and without restriction or condition released to the public upon issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR1.808. Further, the record must be clear that the deposit will be maintained in a public depository for a period of 30 years after the date of the deposit, 5 years after the last request for a sample or for the enforceable life of the patents whichever is longer. See 37 CFR 1.806.

If the deposit has not been made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the cell line has been deposited at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been

met. Amendment of the specification to disclose the date of deposit and the complete name and address of the depository is required.

Applicant should disclose the address for the DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it recites a test system consisting of cells expressing a heterologous P4502D6 allele wherein at least three alleles are expressed in said test system, but as the claim is written it is not clear whether the alleles are all expressed in one cell or each allele is expressed in an individual cell.

Claim 1 is vague and indefinite because it recites the phrase " in a heterologous manner" and the metes and bounds of what constitutes "a heterologous manner" are not clear.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat.

App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation "a cytochrome P450 2D6", and the claim also recites "hCYP2D6" which refers specifically to human CYP2D6 and which is the narrower statement of the range/limitation.

Claim 2 is vague and indefinite because it recites the phrase " in a population" and the metes and bounds of what constitutes "a population" (i.e. cells, or animals containing cells) are not clear.

Claim 5 is vague and indefinite because it recites the phrase "cell derived therefrom" and the metes and bounds of how the cell can be derived from fibroblasts are not clear.

Claims 9-13 provide for the use of a test system, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 15 is vague and indefinite because it recites that cells expressing the alleles in question are tested "with respect to the cytochrome P450 2D6-dependent

metabolism of compounds" and it is not clear what is meant by "testing the cells with respect to metabolism". Furthermore, claim 15 recites "metabolism of one or more compounds" and then recites "comparison of the metabolism of the cells" and the metes and bounds of "metabolism of the cell" are unclear. For example it is not clear if the claim is drawn to the specific metabolism of selected test compounds to breakdown products, or if by reciting "metabolism of the cells" the claim is drawn to multiple metabolic processes within the cells to be compared.

Claim 16 recites the limitation "the cytochrome P450 content". There is insufficient antecedent basis for this limitation in the claim. As a result, it is not clear what cytochrome P450 content is being quantified (i.e. from a cell, a synthetic peptide, etc.).

Claim 16 is vague and indefinite because it recites solubilization of cytochrome P450 by means of non-ionic detergent, and the metes and bounds of "by means of" are not clear.

Claim 17 recites the limitation "cell homogenate" in step (a) and (b). There is insufficient antecedent basis for this limitation in the claim. Claim 17 dependent on claim 16 and there is no cell homogenate or cells recited in claim 16.

Claim 17 recites the limitation "the reduced spectrum" in step(d). There is insufficient antecedent basis for this limitation in the claim and it is not clear what reduced spectrum is intended

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 9 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (Drug Metab. Disp. 1999. Vol. 27(3). Pp385-388).

Wang et al teach that they found 3 alleles of a CYP2D6 gene in the Chinese population which were cloned and transfected into Rat-1 cells (see page 387, right column, 2nd full paragraph and Figure 4, in particular) which reads on a test system consisting of cells expressing at least 3 alleles of a heterologous cytochrome P450 2D6. or a kit containing said test system. Wang et al teach that the metabolic activity of the alleles was tested by assay for formation of 1-hydroxy-bufuralol by addition of bufuralol to microsomes prepared from cells expressing the alleles, see page 386, right column, 1st full paragraph and figure 4, for example) which reads on a method for the screening of substances with respect to their metabolization by human cytochrome P450 2D6 by contacting cell of the test system with the substance and the metabolic product is measures.

Claims 16 and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,356,806 (Harris et al).

Harris et al teach measurement of CO-reduced difference spectra comprising solubilization of cytochrome P450 from cell lysate microsomal fractions with emulgen 913, centrifugation and measurement of CO-reduced difference spectra (see column 11, lines 5-18, column 13, lines 35-45, for example) which reads on a method for quantification of cytochrome P450 content wherein said method comprises the solubilization of cytochrome P450 by means of the non-ionic detergent emulgen 913, centrifuging the solubilizate and measurement using CO difference spectra.

Harris et al also teach that to determine the spectral characterization of cytochrome P450, microsomes were solubilized with emulgen 913, centrifuged and the supernatant was used to determine a dithionite reduced spectra and a CO saturated spectra (see column 3, lines 40-45, column 13, lines 33-54, and Fig.4, in particular), which reads on a method comprising preparation of cell homogenate, addition of emulgen 913 to the cell homogenate, removing insoluble material, determination of the reduced spectrum, saturation with carbon monoxide, measurement of the CO/reduced spectrum, evaluation of the cytochrome P450 content by means of the spectra.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura McGillem whose telephone number is (571) 272-8783. The examiner can normally be reached on M-F 8:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Laura McGillem
12/27/2005

DAVID GUZO
PRIMARY EXAMINER